19 Sick cell disease

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INTRODUCTION

Hemoglobinopathies complicating pregnancy number in the hundreds, but fortunately most of them are very rare (1). These inherited disorders usually result from structural abnormalities such as additions, deletions, or substitutions in the amino acids that comprise the two pairs of polypeptide chains common to each hemoglobin molecule (Table 1). These amino acid linkages contain either 141 or 147 amino acids, are responsible for the nomenclature, and comprise the common types of hemoglobin such as A, A₂, F, and so on (2).

Sickle cell disease (SCD) refers to a group of autosomal recessive disorders involving abnormal hemoglobin (hemoglobin S). Hemoglobin S differs from the normal Hb A because of a single nucleotide substitution of thymine for adenine in the globin gene. This alteration causes a substitution of valine for glutamic acid in the number six position of the globin polypeptide. Asymptomatic individuals with heterozygous Hb S genotypes (carriers) are said to have sickle cell trait. The most severe form of the disease, Hb S-S (homozygous Hb S), is called sickle cell anemia (3).

Sickle cell crisis occurring at any time during gestation is a medical emergency (4). Vaso-occlusive sickle cell crisis is the most common maternal complication noted in gestations complicated by sickle hemoglobinopathies (5). Crisis is associated with increased maternal and perinatal morbidity and mortality (6). Severity as well as frequency of crises among pregnant women is extremely variable and may occur during the prenatal or intrapartum period as well as the puerperium (7). Improvements in management over the last two decades have resulted in improved outcome for such women and their progeny. Nevertheless, providers who care for these high-risk patients must be prepared to practice preventive medicine, recognize the early signs of crisis, and respond rapidly with a well-founded perinatal management plan.

EPIDEMIOLOGY

In the United States, sickle cell anemia affects about 70,000 people (8). It mainly affects African-Americans. The disease occurs in about 1 out of every 500 African-American births. Sickle cell anemia also affects Hispanic Americans. The disease occurs in 1 out of every 36,000 Hispanic American births (8,9). Patients with Hb S-S, as well as with other variants, such as hemoglobin S-C (Hb S-C) and hemoglobin S- β thalassemia (Hb S- β Thal), are said to have SCD and this is most often responsible for adverse effects on the mother, the fetus, and the newborn (3). These are also the disorders most likely to be associated with sickle cell crisis. Other sickle hemoglobinopathies such as Hb S-D, Hb A-S, and Hb S-E are unlikely to result in sickling episodes.

SICKLE CELL TRAIT

About 2 million Americans have sickle cell trait. The condition occurs in about 1 in 12 African-Americans (8). Sickle cell trait has been considered to be an essentially benign condition during pregnancy, with few exceptions (10,11). A common problem tends to be an increased rate of urinary tract infections, thought to be associated with an inability to concentrate urine and asymptomatic bacteriuria among patients with sickle cell trait. There is some literature that contradicts the benign nature of the carrier state revealing an increased risk of intrauterine fetal demise, spontaneous miscarriage, and intrauterine growth restriction (12,13). However, due to a lack of sufficient evidence, routine obstetrical management with monthly urinalysis is the only recommendation in this group of patients at this time.

MORBIDITY AND MORTALITY

Patients with Hb S-S or Hb S-C have no hemoglobin A, therefore the predominant hemoglobin is Hb S, 90% to 95%, with the remainder being Hb F. Patients with this disorder have been shown to have a shorter life span, more common infections, and when pregnant, a higher maternal as well as perinatal mortality/morbidity (1). The fertility rate does not appear to be decreased unless there are frequent crises and disseminated disease affecting many systems. Due to improvements in modern medicine, the maternal death rate has been reduced to less than 2%, and many women are now electing to proceed with pregnancies (14).

Women with SCD are at an increased risk to experience both medical complications (such as infections, thromboembolic events, and stroke) and pregnancy-related complications (such as pre-eclampsia, eclampsia, preterm labor, placental abruption, and fetal growth restriction). The risk for experiencing these complications is significantly higher than that in other women (15,16). Decreased placental blood flow due to sickling in the tortuous, arcuate vessels of the myometrium has been associated with poor perinatal outcomes (2). More than one-third of pregnancies in women with SCD terminate in miscarriage, stillbirth, or neonatal death, according to the National Institutes of Health Cooperative Study of Sickle Cell Disease (17). The neonatal mortality rates are not increased in patients with SCD per se but may appear to increase due to preterm deliveries.

These women are also more likely to experience pneumonia, pyelonephritis, postpartum infection, sepsis, and systemic inflammatory response syndrome compared with women without SCD. At the time of delivery, these women are also more likely to have asymptomatic bacteriuria and genitourinary infections (15). Severe cardiopulmonary ailments may be observed in those women with long-standing disease. Cardiovascular sequelae are often a consequence of chronically

Table 1 Normal/Abnormal Hemoglobin				
Hemoglobin classification	Globin defect	Chain present	Common name	Hematologic destination
Adult hemoglobin ^a	None	2a 2b	Hb A	a ₂ ^A d ₂ ^A
Adult hemoglobin ^a	None	2a 2d	Hb A ₂	a ₂ ^A d ₂ ^A
Adult fetal hemoglobin ^a	None	2a 2g	Hb F	a ₂ ^A g ₂ ^F
Sickle hemoglobin ^b	b-chain substitution	2a 2b	Hb S	a ₂ ^A b ₂ ^S (6 glu ® val)
C-hemoglobin ^b	b-chain substitution	2a 2b	Hb C	a ₂ ^A b ₂ ^C (6 glu ® lys)
Methemoglobin ^b	a-chain substitution	2a 2b	Hb M Boston	a ₂ ^M (58 his ® tyr)b ₂ ^A
b-Thalassemia ^a	None (decreased synthesis)	2a 2b	Hb B Thal	a ₂ ^A b ₂ Thal

^aStructurally normal. ^bStructural abnormalities include substitution, inversion, or deletions of amino acids in either chain.

Figure 1 Blood film in patient with sickle cell crisis.

high cardiac output due to anemia, although these women rarely die of heart disease, but almost all eventually have some degree of ventricular dysfunction from hypertrophy and diastolic dysfunction. These underlying changes make affected women less tolerant of the additional increase in cardiac output noted in pregnancy (18). Pulmonary hypertension is acknowledged increasingly as a complication of SCD. It has been described in up to 30% of this population and is associated with a high mortality rate (19). The statistically significant presence of pulmonary hypertension at delivery supports the previous observation and warrants the need for appropriate evaluation and management.

Although neonates are asymptomatic at birth because of a higher concentration of hemoglobin F, the incidence of neonatal mortality increases after about 6 months with 20% of overall deaths from SCD occurring in the first 2 years, 10% between the ages of 2 and 5 years, and the remainder between 5 and 30 years (20). During pregnancy, severe anemia is the rule among patients with SCD and rarely does the hematocrit rise above 25%. Infections are also common and usually involve the urinary tract, pulmonary system, and orthopedic system.

Diminished oxygenation in the intravascular compartment in patients with SCD converts the normal oval red blood cells

into the classic sickle-shaped erythrocytes noted in subjects undergoing crisis (Fig. 1). These sickle cells lodge in the microvasculature of many organs and result in a decreased life span of red blood cells as well as the maternal and perinatal complications mentioned above. Any event leading to deoxygenation can initiate a sickle cell crisis. For instance, infections from viruses or bacteria, acidosis, dehydration, trauma, blood loss, severe stress, strenuous physical activity, high altitude, and hypothermia have been incriminated.

There are several different kinds of sickle cell crisis. The most common is the vaso-occlusive crisis, which is most frequently noted in pregnant women and adults. The less common hematologic type of crisis is more often seen, but not exclusively so, in children (Table 2). The clinical expressions of the vaso-occlusive crises are extremely variable in their presentation but usually follow a characteristic pattern in each patient. These recurrent and sudden attacks of pain most often involve the abdomen, extremities, central nervous system, and chest although no body area is immune from these attacks (21). Some patients exhibit generalized pain and malaise, while others have more localized syndromes involving a compromised microcirculation in various areas of the body.

Table 2 Sickle Cell Crisis Classification

<i>Vaso-occlusive</i>
Abdominal
Chest
Joints
Central nervous system
<i>Hematologic</i>
Aplastic
Hemolytic
Megaloblastic
Splenic sequestration

On the other hand, hematologic crises are infrequent among pregnant women, but if they occur, aplastic crisis is the most common type. Fortunately, this type of crisis is usually self-limited and most often associated with infection. Hemolytic crises, in general, are most commonly related to concomitant spherocytosis or glucose-6-phosphate dehydrogenase deficiency. Megaloblastic crises are usually secondary to folate depletion and are remedial to supplementation. Finally, splenic sequestration crises are usually limited to childhood. As a group, hematologic crises are characterized by sudden anemia without icterus, pale conjunctiva, malaise, reticulocytopenia, and cardiopulmonary failure.

ETIOLOGY

In a patient with SCD, the symptom constellation of the chronic, severe anemia and frequent pain leads one to suspect a vaso-occlusive crisis. Most commonly, this event in the pregnant adult is associated with apparent or occult infection (20–33%) (21). Pneumonia, urinary tract infection, and puerperal endomyometritis, as well as osteomyelitis, are the infectious sites commonly encountered with sickle cell crisis. *Pneumococcal pneumonia* or meningitis is particularly frequent in adolescent pregnant patients with SCD (22). Gram-negative bacteria, such as *Escherichia coli* or *Salmonella*, are the most common organisms noted in the third decade of life (4). These organisms are particularly likely to attack the renal and gastrointestinal (gallbladder) systems, respectively. During the second decade of life, *Mycoplasma pneumoniae* is also common.

Factors other than infection have been associated with vaso-occlusive crisis in these patients. Acidosis from dehydration and hypotension has been noted to initiate such crises (1). Strenuous activity, as well as drug overdose and hypothermia, have likewise been associated with these events (2). Therefore, when confronted with a suspected vaso-occlusive crisis in a parturient with SCD, one should suspect infection first but rule out other factors during intensive assessment.

PATHOPHYSIOLOGY

The variable clinical symptoms with which these patients present is not fully explained. There is evidence to suggest that this variability may be related to the presence of linked and unlinked genes, which modify the disease expression (23). Another theory has been that of incomplete penetrance. As previously noted, the molecular basis for sickle cell crisis can be traced to the single amino acid substitution in the sickle hemoglobin molecule, which distinguishes it from hemoglobin A. During deoxygenation or under conditions of acidosis

as well as hypoxia, the molecules of Hb S aggregate in a process called nucleation.

Hydrophobic bonding occurs between the abnormally substituted valine, owing to the change in electromagnetic charge. These hydrophobic bonds lead to the formation of polymerized hemoglobin strands, which become tactoids and microcables that eventually transform the cell into the half-moon or crescent shape (Fig. 1) (24). This overall process of gelation of the sickle hemoglobin is enhanced by increasing levels of sickle hemoglobin and/or 2,3-diphosphoglycerate levels. It is reduced by lowering the oxygenation or pH (25).

Repetitive cycles of gelation during the red blood cell life cycle distort the cellular membrane, with resultant potassium and water reduction as well as calcium accumulation and membrane fragmentation (24). This leads to an increase in the intracellular hemoglobin concentration with a concomitant increase in membrane rigidity to form discocytes or irreversibly sickled (26). The irreversibly sickled cells retain the half-moon shape despite oxygenation. These irreversibly sickled cells constitute up to 50% of the red cell mass in such parturients. However, the index of reversible/irreversible sickle cells does not appear to correlate well with vaso-occlusive crisis or its severity, but does have a positive relationship to the degree of anemia.

These abnormalities of the red cells themselves do not, alone, explain the pathophysiology of the sickle cell crisis. It is currently felt that there exists a combination of the erythrocyte abnormalities, plasma flow alterations, and vessel wall interactions that are associated with sequestration and destruction of abnormal red cells in the microcirculation (Fig. 2) (27). This would explain patient variability noted in the clinical expression of a sickle crisis. Another factor involved in the pathophysiology of sickle cell crisis appears to be the large oscillation in blood flow in the microcirculation (28). With the use of laser-Doppler velocimetry, rather large changes in blood flow in factors of 7–10 s with peak/trough magnitudes measured at 50% of mean flow were noted. These findings would suggest that during sickle cell crisis, there is periodic flow in the microcirculation with synchronized rhythmic oscillations versus the continuous even-flow pattern observed in patients with normal hemoglobin.

Therefore, although the environmental factors may stimulate deoxygenation resulting in aggregation, polymerization, and subsequent formation of sickled red cells, flow dynamics and also microcirculation factors are important determinants of the crisis cycle (Fig. 2). These factors combine to increase whole blood viscosity and, thus, alter vasomotion in the microcapillaries. This would lead to sludging and destruction of red cells in the microcirculation. This promotes further deoxygenation, which leads to vascular injury via ischemic necrosis, which results in pain and the other symptoms expressed during vaso-occlusive crises.

The marked susceptibility of parturients with sickle hemoglobinopathies to infection is related to functional hyposplenism, defective activation of complement fixation, decreased serum IgM, impaired serum opsonizing capacity, and defective granulocyte phagocytosis (29). There does not appear to be any difference in the percentage of helper or suppressor T cells or B cells in subjects in crisis (30). This finding is compatible with the observation that patients with sickle hemoglobinopathies did not show increased susceptibility to those infections that are normally associated with depressed cell-mediated immunity (31).

Figure 2 Vicious cycle of sickle cell crisis. Abbreviation: 2,3 DGP, 2,3-diphosphoglycerate.

DIAGNOSIS

The diagnosis of hemoglobinopathies, including sickle cell disorders, is made by hemoglobin electrophoresis. In the homozygous form, nearly all the hemoglobin is Hb S with small amounts of Hb A₂ and Hb F. Heterozygous sickle cell trait (Hb AS) is identified by a larger percentage of Hb A and an asymptomatic course. Solubility tests (Sickledex) alone are inadequate for the diagnosis of sickle cell disorders because they cannot distinguish between the heterozygous AS and homozygous SS genotypes. In addition, they fail to detect other pathologic variants such as Hb C trait, thalassemia trait, Hb E trait, Hb B trait, and Hb D trait (3).

Although some tests for crisis are helpful, the diagnosis is largely a clinical experience and basically one of exclusion. Fortunately, most women with sickle hemoglobinopathies are known prior to pregnancy. For patients with SCD, the first step is to confirm the diagnosis with hemoglobin electrophoresis. Once the diagnosis is documented, surgical/medical/obstetric conditions associated with a similar symptom complex or even malingering must be ruled out (Table 3). Because a parturient may have any one of many medical, surgical, or obstetric complications, pain in a pregnant woman with SCD does not always result from vaso-occlusive crisis.

Infection and crisis are usually associated with an increase in the segmented neutrophil counts as well as the presence of bands. A hemolytic crisis with anemia is presumed in the presence of an elevated lactate dehydrogenase, a reticulocyte count of 3% to 15%, an elevation in unconjugated bilirubin, and a low serum haptoglobin.

MANAGEMENT
General

Pregnant patients with SCD need increased prenatal folic acid supplementation. The standard 1 mg of folate in prenatal vitamins is not adequate for patients with hemoglobinopa-

Table 3 Differential Diagnosis of Sickle Cell Anemia
<i>Obstetric factors</i>
Threatened abortion
Preterm labor
Placental abruption
Uterine rupture
Ectopic pregnancy
Degenerating leiomyomata
Ovarian torsion
Pregnancy-induced hypertension
<i>Medical factors</i>
Renal/ureteral colic
Cystitis
Pyelonephritis
<i>Other factors</i>
Pneumonia
Pulmonary embolism
Arthritis
<i>Surgical factors</i>
Cholecystitis
Cholelithiasis
Appendicitis
Pancreatitis
Peptic ulcer disease
Perforated viscus
Intestinal obstruction
Volvulus
Ischemic colitis
<i>Malingering</i>
Drug addiction

thies; 4 mg/day of folic acid should be prescribed because of the continual turnover of red blood cells (3). Supplemental iron is not usually recommended due to the risk of iron overload that accompanies chronic hemolysis and transfusions. Its administration can be considered if serum iron and

ferritin are found to be diminished. Routine prenatal labs including evaluation for the hepatitis B antigen and HIV should be performed at the patient's initial visit. Other labs to consider would be serum uric acid, creatinine, liver function tests, and a 24-hour urine collection for protein and creatinine to assess for the presence of preexisting vascular disease. If not already accomplished, the patient should be immunized with both the pneumococcal and meningococcal vaccines due to the likelihood of autosplenectomy during childhood and their susceptibility to encapsulated organisms. Neither vaccine is contraindicated in pregnancy.

Intrauterine growth restriction, reduced birth weight, and lower placental weights are common with this disease and may be due to vascular changes within the uteroplacental unit as well as preterm delivery (32,33). It is likely that chronic vascular occlusion, even in the absence of clinically overt pain crisis or acute chest syndrome, contributes to placental injury and adversely affects fetal growth. Altered vascular flow rather than anemia may account for low birth weights in infants of women with Hb S-S, which does not appear to improve with transfusion support (14). Starting at 24 to 28 weeks, monthly ultrasonography is recommended to assess fetal growth, and patients should be instructed in daily fetal movement counts. Nonstress testing and biophysical profile testing should be considered weekly beginning at 32 to 34 weeks. Doppler ultrasound, performed at 28 to 30 weeks to assess umbilical artery flow and systolic/diastolic ratios as a predictor of intrauterine growth restriction, may be a useful adjunct.

Despite advances during the past 20 years and the appreciation of the molecular basis of sickle cell crisis, there is no specific therapy available. However, an understanding of the pathophysiology involved in vaso-occlusive crisis allows the provider to address those aspects of this event that can be treated. Such therapeutic regimens generally include (i) adding fluids to reduce intracellular hemoglobin concentration, (ii) correcting acidosis when present, (iii) treating infection, and (iv) increasing oxygen concentration.

Antepartum

During the prenatal period when the patient in crisis is not in labor and is remote from term, hospitalization in a quiet area where bed rest, analgesia, and hydration can be carried out is optimal. Because of the risk of fetal loss, health assessment via biophysical profile and/or fetal heart rate monitoring is carried out during crisis treatment if gestational age is sufficient to consider intervention for fetal distress. In addition, continuous fetal heart rate monitoring is helpful, because resolution of worrisome signs, such as late decelerations, has been demonstrated during the treatment of sickle cell crisis with blood infusion (34).

Initial medical assessment should focus on detection of the following medical complications requiring specific therapy: infection, dehydration, acute chest syndrome (fever, tachypnea, chest pain, hypoxia, radiologic chest infiltrates), severe anemia, cholecystitis, splenic enlargement, abdominal crisis, and neurologic events (cerebral infarct, cerebral hemorrhage, transient ischemic attack, seizure). Vigorous rehydration is useful, particularly in crisis patients who are febrile (4). In the absence of cardiopulmonary disease, infusion of a liter of Ringer's lactate or isotonic saline during the first 2-hour period with continuing replacement at 125 mL/hr is undertaken.

Careful monitoring of intake and output is essential, but invasive hemodynamic monitoring and urinary catheterization are usually avoided, because of the risk of infection. The administration of alkali during the hydration process has not been found to be helpful (35). For analgesia, opiates are superior to nonsteroidal agents in the presence of severe pain. Opiates are not associated with teratogenicity, congenital malformations, or toxic effects other than transient suppression of movement and variability in fetal heart tones. Chronic exposure to opiates, such as that in women who require methadone or other medications to control severe chronic pain, can result in neonatal abstinence syndrome after birth. Acetaminophen is preferable if mild analgesia is required. As soon as the pain begins to regress, nonnarcotic agents are recommended. It is important to recognize that assessment of fetal well-being during a pain episode may be complicated by the use of opiates to treat sickle cell crisis pain, which transiently affect nonstress testing and biophysical profile scores (36). Caution must be used when interpreting the results of these tests during an acute pain episode, because they may not be predictive of increased perinatal morbidity and mortality in the absence of other findings (14).

Although the utility of oxygen therapy is unproven, it is often employed during crisis. Oxygen is administered at 3–6 L/min by tight face mask or nasal cannula. Arterial blood gas assessment is usually recommended if hypoxemia is suspected. Because infection is present in up to one-third of patients with vaso-occlusive crisis and since it is frequently associated with maternal death occurring in sickle cell crisis, attempts to detect occult infection are undertaken immediately. If an infection is suspected, then broad-spectrum antibiotic therapy is begun after appropriate cultures are obtained. Prophylactic antibiotic use, however, is not generally recommended.

BLOOD TRANSFUSION

Controversy exists regarding the role of prophylactic blood transfusion in the management of SCD in pregnancy (37–41). In the only randomized controlled trial published to date, prophylactic transfusion was associated with a decreased risk for painful crisis and severe anemia, but no difference was observed for pregnancy outcome (38). By limiting transfusion to situations in which it is clinically indicated, patients are not subjected to the increased risk for blood-borne infections, iron overload, and alloimmunization. The rate of alloimmunization in sickle cell patients is estimated to be between 18% and 36% (42). It is estimated that six to eight deaths per year in the United States occur as a result of delayed transfusion reactions (43). It appears from the available evidence that the reduction in morbidity and mortality of SCD in pregnancy may be attributable to improvements in general management of pregnancy rather than prophylactic transfusion per se (3).

However, prophylactic transfusions may be indicated in patients who have particularly severe disease manifestations or for symptomatic patients who are unresponsive to conservative management (44). Major complications (e.g., worsening anemia; intrapartum complications such as hemorrhage, septicemia, and cesarean delivery; painful crisis; chest syndrome) may require intervention with an exchange transfusion. There is no consensus regarding the exact hematocrit value below which transfusion should be considered. However, when a transfusion is clinically indicated in the patient with SCD, the

Table 4 Manual Partial Exchange Transfusion

Measure hemoglobin A level and hematocrit
Type and match six units packed red blood cells
Start intravenous administration of 1L normal saline (200–400mL in the first hour) then 150–250mL/hr
Phlebotomize 500mL blood from opposite arm over 30 min
Give two units leukocyte-poor washed red cells (under pressure and warmed) over 1–2 hours
Repeat procedure after 4 hours
If hematocrit 35% and hemoglobin A 50%, discharge home
If hemoglobin A <50%, repeat procedure

objective is to lower the percentage of Hb S to approximately 40% while simultaneously raising the total hemoglobin concentration to about 10g/dL (3).

Exchange transfusion, also known as erythrocytapheresis, allows the Hb S-containing cells and irreversibly sickled cells to be removed by extracorporeal, differential centrifugation. It affords the simultaneous return by venous access in the other arm of the patient's own plasma, leukocytes, platelets, and clotting factors along with donor, leukocyte-poor washed Hb A-containing red cells. This type of transfusion occurs via a machine that allows for automated continuous erythrocytapheresis. In addition, this method maintains isovolemia at all times and allows the provider to accurately monitor the patient's hematologic indices such as hemoglobin levels and hematocrit. It also has the advantage of administration on an outpatient basis. If such a device is not available, the manual "push–pull" mechanism can be considered (Table 4) (45).

Generally, six units of donor packed red cells are exchanged by this process and there is rapid resolution of crisis symptomatology and ongoing sickling. In addition to being more isovolemic, automated continuous erythrocytapheresis requires less transfusion time than the manual method (46).

Obviously, most of the complications associated with this approach are related to the risk of the blood products. Blood products given to these patients should be from cytomegalovirus-seronegative donors or leukoreduced. Careful cross-matching to minimize minor blood incompatibilities and alloimmunization is critical in avoiding problems later for these patients who may need blood products at various points during their life. The use of blood from family members or friends matched for recipient and donor red cell antigens are clinically helpful in reducing the number of post-transfusion crises. Such episodes are known as delayed hemolytic transfusion reactions. The exact mechanism of hemolytic transfusion reaction is not well understood, and the pathophysiology seems to be far more complex because it involves the destruction of both patient and donor RBCs. A subcategory of this problem is known as a delayed transfusion reaction. It is classically characterized by a clinical triad of fever, hyperbilirubinemia, and anemia occurring 3–10 days after transfusion. Laboratory tests that aid diagnosis include increased reticulocyte count, free hemoglobin in the urine, fragmented RBCs on peripheral smear, decreased post-transfusion Hb A on electrophoresis, or discovery of previously undetected alloantibodies (47).

Intrapartum

The occurrence of a vaso-occlusive crisis during labor offers additional challenges to the provider. Obviously, with painful

uterine contractions, the diagnosis of a vaso-occlusive crisis may be more difficult. If delivery is expected within a short time, a simple transfusion of two units of leukocyte-reduced washed red cells can be considered. During labor, patients should remain in the lateral recumbent position and receive oxygen by tight-fitting face mask. Careful monitoring of maternal and fetal vital signs is essential. Usually, when crisis has been diagnosed during labor and late decelerations appear, infusion of blood products has been associated with resolution of suspected fetal hypoxemia. Maternal blood gas assessment, if necessary, is carried out, but invasive hemodynamic monitoring is avoided unless other concomitant disease processes such as pre-eclampsia, and so on, are present. Urinary catheters, as well as intrauterine catheters, are discouraged, because of their association with increased infection.

No consensus exists concerning the anesthetic care of parturients with SCD (48–50). It appears that the use of general anesthesia can result in a significant increase in postpartum sickling complications (51). We feel that epidural analgesia/anesthesia is ideal if the vaso-occlusive crisis is mild or can be aborted with blood infusion. If not, intermittent intravenous analgesia with pudendal block for vaginal delivery may be appropriate. Continuous epidural morphine has also been utilized with success in these patients. If cesarean delivery is indicated, the choice of regional or general anesthesia depends on the patient's general condition and the preference of the anesthesiologist. Careful monitoring of the patient's vital signs is important during anesthesia so that hypoxemia and acidosis are obviated. Avoidance of hypothermia and hypoxia during labor, as well as in the delivery room, is critical. Persons skilled at neonatal resuscitation should be present at delivery. Consultation with anesthesia and neonatology during labor is important. The use of oxytocic agents for induction/augmentation or an ecobolic agent during the third stage of labor is not contraindicated.

Postpartum

Crises in Hb S-S women after delivery usually do not develop unless hypovolemia, acidosis, or infection occurs. On the other hand, patients with Hb S-C are more likely to experience crises postpartum than during pregnancy. The same pitfalls of management applied during the antepartum period are also prudent after birth. Both urinary tract infection and endometritis are common and are frequently associated with crises. There is also a substantial increased risk of pulmonary edema and thromboembolic disease in these patients. Maintenance of isovolemia and high Hb A levels (>20%) appear to be important points in management.

SUMMARY

Overall, pregnant women with SCD appear to be more likely to experience antepartum, intrapartum, and postpartum complications when compared with unaffected women. Access to high-risk obstetric care, patient education, and close follow-up are important to minimize maternal morbidity and mortality.

In the absence of consistent data supporting a reduction in adverse obstetric or fetal outcomes, the use of transfusion therapy is generally limited to patients who experience a significant increase in SCD activity with severe complications, including acute chest syndrome, acute severe anemia (Hb <5.0–6.0 g/dL), severe, or refractory pre-eclampsia, and those

who are in anticipation of surgery (14,52). A high index of suspicion and good diagnostic acumen is necessary to obtain optimal results in the pregnant patient with SCD.

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